

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 24 July 1998 (24.07.98)	Applicant's or agent's file reference 1581F PCT
International application No. PCT/US97/21054	Priority date (day/month/year) 05 December 1996 (05.12.96)
International filing date (day/month/year) 14 November 1997 (14.11.97)	
Applicant CLARK, Abbot, F. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

01 July 1998 (01.07.98)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer B. Fitzgerald</p> <p>Telephone No.: (41-22) 338.83.38</p>
--	---

PATENT COOPERATION TREATY

COPY

PCT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KELLER, Günter
LEDERER, KELLER & RIEDERER
Prinzregentenstrasse 16
D-80538 München
ALLEMAGNE

WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day, month, year)

16. 09. 98

Applicant's or agent's file reference
1581F PCT

REPLY DUE

within 3 months, ~~days~~
from the above date of mailing

International application No.

PCT/US 97/ 21054

International filing date (day, month, year)

14/11/1997

Priority date (day, month, year)

05/12/1996

International Patent Classification (IPC) or both national classification and IPC

C12Q1/68

Applicant

CLARK, Abbot, F. et al.

1. This written opinion is the 1st (first, etc.) drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 05/04/1999

Name and mailing address of the IPEA:



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Netherlands
Tel.: (+ 31-70) 340-2040, Tx. 31 651 epo nl
Fax: (+ 31-70) 340-3016

Authorized officer

Examiner Molina Galan E.

Formalities officer
(incl. extension of time limits)
Telephone No.

C. Cardenas

WRITTEN OPINION

International application No.

PCT/US97/21054

I. Basis of the opinion

1 This opinion has been drawn up on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

☒ the international application as originally filed

☐ the description, pages

.as originally filed

pages

.filed with the demand

pages

. filed with the letter of

☐ the claims, Nos.

.as originally filed

Nos.

.as amended under Article 19

Nos.

. filed with the demand

Nos.

. filed with the letter of

☐ the drawings, sheets / fig.

.as originally filed

sheets / fig.

. filed with the demand

sheets / fig.

. filed with the letter of

2. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.

☐ the drawings, sheets / fig.

3 ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2 (c)).

4 Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Claims
	Claims
Inventive Step	Claims
	Claims
Industrial Applicability	Claims
	Claims

2. Citations and Explanations

2.1 CITATIONS

Reference is made to the following documents:

- D1: WO- A- 96/14411, University of California
D2: J. Glaucoma, 4, 1995, 354- 369, Abbot F. Clark
D3: J. Biol. Chem., 271, 4- 1996, 9550- 9559, Oakley et al.

2.2 NOVELTY (Art. 33(2) PCT)

- 2.2.1 The present application does satisfy the criterion set forth in Article 33(2) PCT because the subject- matter of Claims 1- 5 is new in respect of prior art as defined in the regulations (Rule 64(1)- (3) PCT).

2.3 INVENTIVE STEP (Art. 33(3) PCT)

- 2.3.1 Document D1 is considered to represent the most relevant state of the art and discloses a method for diagnosing glaucoma which comprises detecting aberrant expression or mutations (defects) of the trabecular meshwork induced glucocorticoid response (TIGR) gene (cf claims 9 and 33). The subject- matter of claim 1 differs in that diagnosis is based on the β isoform of the glucocorticoid receptor (GR β).

- 2.3.2 The problem to be solved by the present invention may therefore be regarded as providing alternative ways for the detection of glaucoma. The solution would be basing a diagnostic method on the detection of abnormal expression or mutations of the GR β gene.
- 2.3.3 The relationship between glucocorticoid (receptors) and glaucoma (see review in D2, specially from page 359 onwards) and the existence of the β isoform of the glucocorticoid receptor (D3) were known. There is however no indication at all that GR β could be related in any way to glaucoma occurrence and therefore the diagnostic use of it could not have been anticipated and claims 1- 5 involve an inventive step (Art. 33(3) PCT).

(NOTE: the IPEA has made the assumption that TIGR is not the same protein as GR β .)

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

- 1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor is this document identified therein.
- 2 If amendments are filed, it should be by way of replacement pages in the manner stipulated by Rule 66.8(a) PCT. In particular, fair copies of the amendments should be filed preferably in triplicate. Moreover, the applicant's attention is drawn to the fact that, as a consequence of Rule 66.8(a) PCT the examiner is not permitted to carry out any amendments under the PCT procedure, however minor these may be.
- 3 In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT). If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.
- 4 The applicant is requested to note that in accordance with Rule 66.4 (a) PCT the issuance of an additional Written Opinion (WO) is facultative. Moreover, as the final action in the PCT procedure is an International **Preliminary** Examination Report (IPER) and not a decision, a violation of the right to be heard cannot exist. The applicant can not therefore rely on obtaining a second WO before the IPER is issued and is requested to answer this first WO in a complete manner.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The claims are not clear because the term $GR(\beta)$ is ambiguous. It should be substituted by the complete name as defined in the description.

LEDERER, KELLER & RIEDERER

Patentanwalte - European Patent Attorneys

European Patent Office

80298 München

COPY

DR. A. VANDER WERTH
(1934 - 1974)

DR. FRANZ LEDERER
Dipl.-Chem. München

DR. GUNTER KELLER
Dipl.-Biol. München

DR. MICHAEL BEST
Dipl.-Chem. München

ANTON FRH. RIEDERER v. PAAR
Dipl.-Ing. Landshut

80538 MÜNCHEN
Prinzregentenstraße 16
Telefon (089) 21 23 99 0
Telefax (089) 21 23 99 22
E-Mail lederer_keller@compuserve.com

Dec. 14, 1998
K/sm

CHAPTER II

Re: PCT Application No. PCT/US97/21054
European Patent Application No. 97.947569.6
CLARK Abbot F. et al.
Ref.: 1581F PCT

This is in response to the written opinion dated September 16, 1998.

It is noted with pleasure that novelty, inventive step and industrial applicability of the claims presently on file could be acknowledged.

In order to comply with the suggestion of the International Preliminary Examining Authority a slightly amended set of claims is submitted in triplicate.

In claim 1 the complete name of GRB as originally disclosed on page 2, lines 10 and 11 of the specification has been included into the claim.

Moreover, a new page 1a of the specification is submitted wherein document D1 as mentioned in the written opinion has been duly acknowledged.

Since all objections have been complied with the early issuance of a favourable Preliminary Examination report is earnestly solicited.

gez. Dr. G. Keller

Encl.
set of claims, 3-fold
page 1a of specification, 3-fold

PATENT COOPERATION TREATY

PCT

REC'D 19 MAR 1999

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)


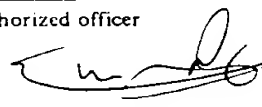
Applicant's or agent's file reference 1581F PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US 97/ 21054	International filing date (day, month, year) 14/11/1997	Priority date (day, month, year) 05/12/1996
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant CLARK, Abbot, F. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This **REPORT** consists of a total of 4 sheets, including this cover sheet.
- ☒ This report is also accompanied by **ANNEXES**, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 01/07/1998	Date of completion of this report 17.03.99
Name and mailing address of the IPEA:  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Netherlands Tel.: (+ 31-70) 340-2040, Tx. 31 651 epo nl Fax: (+ 31-70) 340-3016	Authorized officer  Molina Galan E. Telephone No. 340 3560

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US97/21054

I. Basis of the report

1. This report has been drawn up on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*

☐ the international application as originally filed

☒ the description. pages 1 and 2 . as originally filed
 pages . filed with the demand
 pages 1a . filed with the letter of 14.12.98

☒ the claims. Nos. . as originally filed
 Nos. . as amended under Article 19
 Nos. . filed with the demand
 Nos. 1-5 . filed with the letter of 14.12.98

☐ the drawings. sheets / fig. . as originally filed
 sheets / fig. . filed with the demand
 sheets / fig. . filed with the letter of

2. The amendments have resulted in the cancellation of:

☐ the description. pages:

☐ the claims. Nos.

☐ the drawings. sheets / fig.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2 (c)).

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Claims	1-5	YES
	Claims		NO
Inventive Step	Claims	1-5	YES
	Claims		NO
Industrial Applicability	Claims	1-5	YES
	Claims		NO

2. Citations and Explanations

2.1 CITATIONS

Reference is made to the following documents:

- D1: WO-A-96/14411, University of California
D2: J. Glaucoma, 4, 1995, 354-369, Abbot F. Clark
D3: J. Biol. Chem., 271, 4-1996, 9550-9559, Oakley et al.

2.2 NOVELTY (Art. 33(2) PCT)

- 2.2.1 The present application does satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of Claims 1-5 is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

2.3 INVENTIVE STEP (Art. 33(3) PCT)

- 2.3.1 Document D1 is considered to represent the most relevant state of the art and discloses a method for diagnosing glaucoma which comprises detecting aberrant expression or mutations (defects) of the trabecular meshwork induced glucocorticoid response (TIGR) gene (cf claims 9 and 33). The subject-matter of claim 1 differs in that diagnosis is based on the β isoform of the glucocorticoid receptor (GR β).

- 2.3.2 The problem to be solved by the present invention may therefore be regarded as providing alternative ways for the detection of glaucoma. The solution would be basing a diagnostic method on the detection of abnormal expression or mutations of the GR β gene.
- 2.3.3 The relationship between glucocorticoid (receptors) and glaucoma (see review in D2, specially from page 359 onwards) and the existence of the β isoform of the glucocorticoid receptor (D3) where known. There is however no indication at all that GR β could be related in any way to glaucoma occurrence and therefore the diagnostic use of it could not have been anticipated and claims 1-5 involve an inventive step (Art. 33(3) PCT).

(NOTE: the IPEA has made the assumption that TIGR is not the same protein as GR β .)

WO 96/14411 discloses a method for diagnosing glaucoma in a patient which comprises determining whether the amount of a trabecular meshwork induced glucocorticoid response protein present in the trabecular meshwork of an eye of a patient exceeds the amount of that trabecular meshwork induced glucocorticoid response protein present in the trabecular meshwork of an eye of an individual who is not suffering from glaucoma, wherein the detection of an excessive amount of the trabecular meshwork induced glucocorticoid response protein is indicative of Glaucoma.

AMENDED SHEET
IPEA/EP /

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12Q 1/68	A1	(11) International Publication Number: WO 98/24932 (43) International Publication Date: 11 June 1998 (11.06.98)
(21) International Application Number: PCT/US97/21054 (22) International Filing Date: 14 November 1997 (14.11.97) (30) Priority Data: 60/033,227 5 December 1996 (05.12.96) US (71)(72) Applicants and Inventors: CLARK, Abbot, F. [US/US]; 5603 Rachel Court, Arlington, TX 76017 (US). WORDINGER, Robert, J. [US/US]; 411 Summit Ridge Drive, Euless, TX 76039 (US). (74) Agents: YEAGER, Sally, S. et al.; Alcon Laboratories, Inc., Patent Dept., Q-148, 6201 South Freeway, Fort Worth, TX 76134-2099 (US).		(81) Designated States: AU, CA, JP, MX, US, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: METHODS FOR DIAGNOSING GLAUCOMA AND DISCOVERING ANTI-GLAUCOMA DRUGS (57) Abstract Methods for diagnosing glaucoma and for screening therapeutic agents for their usefulness in treating glaucoma based on the detection of aberrant expression of beta glucocorticoid receptor (GRbeta).		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		